Article

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Editorial

Patient-Reported Outcomes: time for a new approach?

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Patient-reported outcome (PRO) measurement (e.g. health-related quality of life questionnaires, symptom diaries) can provide a standardised, valid and reliable way of gaining the patients' perspective on 'how they are' or the benefits and limitations of a specific intervention. The insights that patients have concerning their health are important given that aspects of patient-reported quality of life are independent predictors of survival in cystic fibrosis (CF) [1]. Regulatory authorities require the inclusion of PROs in clinical trials as an additional outcome parameter and PRO information is becoming important in labelling claims. It is noteworthy that the top 10 research questions, reached by global consensus of patient and healthcare providers, all require the inclusion of CF-specific PROs to achieve meaningful answers [2]. This represents a significant paradigm shift but capturing data that matters to patients, families and clinicians is challenging. Two of the persistent challenges in CF PRO measurement are a) the development and use of technologies to enable efficient administration, accurate scoring, and the correct interpretation of data and b) being able to accurately measure PROs (or parental proxy assessment) across the entire CF lifespan. These important issues are considered by two papers in this issue of the *Journal of Cystic Fibrosis* [3,4].

PRO measurement largely remains a research endeavour with little uptake in clinical practice. Administering, scoring and interpreting PROs in a busy clinic is difficult. It requires staff time and expertise and the results are not instantly accessible to steer a discussion with the patient or to aid clinical decision making. Paper-based data collection suffers from missing, unreadable data that is prone to scoring/mathematical error. The development of electronic PRO (ePRO) technologies is immensely important in clinical practice and for endpoint assessment in clinical trials. It is a cost-saving, patient-friendly approach to PRO assessment: data collection can occur in clinic, the patient's home, workplace or school. Results can be added to a patient's electronic medical file, alerts triggered by problematic scores and clinicians can track patient/parent-reported symptom/event data over time. Importantly, electronic data capture enhances the integrity and accuracy of the data, makes it logistically easier to collect repeated assessments (daily or at several points over a trial), and is preferred over paper-based data collection by the US Food and Drug Administration (FDA).

There is growing evidence that paper and electronic versions of PROs typically provide comparable data but this requires psychometric evaluation if transferring an original paper-based questionnaire to an electronic mode of administration. *Solé and colleagues* have demonstrated measurement equivalence with paper and electronic administrations of the Cystic Fibrosis Questionnaire-Revised (CFQ-R teen/adult version) [3]. The e-CFQ-R web version is linked to an online database that can be adapted for any electronic devise (smartphone, tablet, computer). Immediately the patient completes

the questionnaire, results are sent to the healthcare team and the data are saved in a centralized, protected database. Real-time patient-reported data are available to the clinician as an adjunct to clinical data. Access to the English and Spanish versions are by independent web addresses provided in the paper. Ultimately, the integration of PRO data within electronic care records as developed by Peckham *et al.* [5], or in CF patient registries would enable efficient patient care and longitudinal research endeavours.

There is a lack of PROs that can be used as endpoints in early intervention studies in CF. Such instruments are time-consuming and painstakingly difficult to develop so the research of *Edwards et al.* reporting on the initial development of a CF-specific, parent-reported instrument for children 0-11 years is welcome [4]. The need for an effective way of data collection is also considered. The instrument takes the form of an electronic (web-based data capture), observational sign/symptom diary containing 17 respiratory and activity signs that parents report the presence or absence of. Results suggest that children aged 7 to 11 years are best reporting for themselves, therefore observational reporting by parents should focus on young children aged 0 to 6 years. Considerable evaluation has yet to determine the final instrument but the development of the scale follows FDA guidance enabling its acceptance as a clinical trial endpoint in infants and young children with CF.

Over the last twenty years we have learned a great deal about measuring patient-reported outcomes in CF, and there are many pitfalls when employing PROs in CF trials [6]. They are typically secondary endpoints and the trial is not powered on them, often making it difficult to draw valid inferences about treatments. However, there are trials that have collected patient-reported respiratory symptom data as the primary endpoint [7,8], employing the only CFQ-R subscale that has been approved by the FDA for use as an endpoint. Scientific, regulatory and pragmatic factors are driving the shift towards ePRO data collection. The development of ePROs is not trivial, yet they are fast becoming the 'gold standard' for PRO data capture in clinical trials. The challenge now is to develop CF-specific, lifespan PROs, utilising new technologies that can deliver real-time, high-quality PRO information. They also need to be acceptable to the regulatory bodies to aid their decisions on cost-effectiveness and ensure the appropriate commissioning of new medicines to improve the lives of people with CF and their families.

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